SPINAL CORD CHANGES IN COMBINED SCLEROSIS.*

By WALTER F. SCHALLER, M. D., San Francisco.

It is the subacute form of spinal disease usually associated with anemia which I have selected for a study of cord changes and related clinical symptomatology. In our experience this affection is of comparatively frequent occurrence in California, much more often seen than disseminated sclerosis, although not nearly so often as tabes dorsalis. My records show an incidence about equal to that of brain tumor. It is of rare occurrence in France, more frequent in Germany, and in England the condition is, I should judge, as often met with as with us. Bramwell, in a recent article, makes the point that this disease occurs usually after the age of 35 years. In a review of my series of cases I find that in most instances the disease occurred beyond 40 years of age, although in a few cases it occurred in the twenties. In regard to sex I find a preponderance of males —in a total of 23 cases there were observed 16 males and 7 females. Bramwell states that in five cases of subacute combined degeneration seen by him all were in males. The recognition of this disease is accredited to Lichtheim in 1887, although Gowers (1886) in a clinical lecture on ataxic paraplegia evidently dealt with this disease. American authors—Putman (1891), Taylor (1895), Dana (1899), contributed to our knowledge of this affection. In 1900, an important article appeared in Brain by Russell, Batten and Collier. More recently, articles have appeared by Hennenberg in Lewandowsky system, Bramwell, and Cadwallader. This latter author, basing a clinical study on a communication of Dejerine—syndrome of the long radicular fibres of the posterior columns of the cord in subacute combined sclerosis—emphasized the importance in testing the deep sensibility, particularly the bone sensibility, which is so early affected in combined sclerosis, the superficial sensibility remaining intact, as a rule in the first stages.

Etiology: The cord degeneration is supposed to be due to some toxin which is also responsible for the blood picture. Whether this toxin is caused by some buccal or gastro-intestinal infection which Dr. William Hunter long ago suspected was the case in pernicious anemia, is at present undecided. I may state, however, that from the symptomatology, clinical signs and post mortem evidence, there is considerable reason to support this point of view.

Hennenberg and Bramwell hold that the degenerations in the cord are not true primary system degenerations, but are rather the coalescent degenerated areas causing a secondary pseudo system degeneration. These degenerations are, however, loosely systematized and furnish, at least at the beginning of the disease, an interpretation of the lesions by the symptomatology. Bramwell further believes that the underlying associated anemia is much more frequently the pernicious form than is commonly supposed. In support of this view he relates a case in which in the presence of cord symptoms, no marked anemia occurred for three years, the patient eventually succumbing, however, to pernicious anemia. In my series there were ten cases of pernicious anemia (severe anemia in which the blood index was 1. or over), four cases of secondary anemia, and six cases in which the blood picture was negative. In three cases, the blood examination was incomplete. In four autopsy cases I have made sections of the spinal cord at different levels.

The histological picture of the lesions is a primary degeneration of the nerve elements and replacement by neuroglia. When the degeneration is acute, vacuolization also occurs. The occurrence of amylaceous bodies is frequent. Scattered throughout the posterior and lateral columns is a diffuse cellular increase of indeterminate nature. Putman speaks of these cells as granule cells and their presence is apparently due to the rapid degeneration of myelin and impairment of circulation. They are not considered to indicate inflammation; in fact, there are no evidences of a general or local inflammatory process in either the cord tissue proper, blood vessels or meninges. Numerous observers have emphasized the fact that Lissauer's zone is spared in the degenerations. The process has been noted to be more frequent in the dorsal cord than in the lowest portions of the cord, and is quite often absent in the sacral region. Likewise the degenerations diminish in intensity rapidly above the cervical cord.

A brief account of my autopsy cases is as follows:

Case 1. J. R. M. Dispensary No. 927. This case corresponds to the classical type of Russell, Batten and Collier. Patient entered Clinic Feb. 28, 1912, age 47 years, complaining of inability to walk on account of weakness in legs and numbness, especially in the right leg.

Onset of trouble said to have followed a fall in June, 1911, and began with numbness in legs, especially the right.

Physical Examination: When seen in hospital, patient was bedridden, suffering from a spastic paraplegia with ataxia. Teeth in poor condition; pain felt on deep palpation over gall-bladder and appendix; knee jerks and ankle jerks lively and hyper-tonus of leg muscles. Babinski and Oppenheim signs positive; pupils equal and react to light and accommodation. Sensibility: In the lower extremities, sensation for touch normal; pain sense somewhat impaired; heat and cold also confused, especially in the outer portion of both legs, but with no definite localization. In the right gluteal region, and the dorsum of the left foot, there are areas of hyper-algesia. Deep sensibility not impaired. (Note in history—no mention of separate tests.) Even at the beginning there appeared to be some impairment of the mentality shown by lack of attention and variation in the account of his illness. The value of the sensibility tests suffer perhaps on this account. As the disease progressed there was mental deterioration, the picture resembling the dementia in paresis and in addition patient was disoriented, suffering with delusions, and hallucinations of sight. Very restless, picked at imaginary objects, talked unintelligently. Loss of sphincter control; edema of legs and marked superficial sensory impairment in same, then loss of tendon reflexes and a picture of flaccid paralysis. Cerebro-spinal fluid for cells negative, globulin slightly increased; Was-

* Read before the forty-sixth annual meeting of the Medical Society of the State of California, Coronado, April, 1917.

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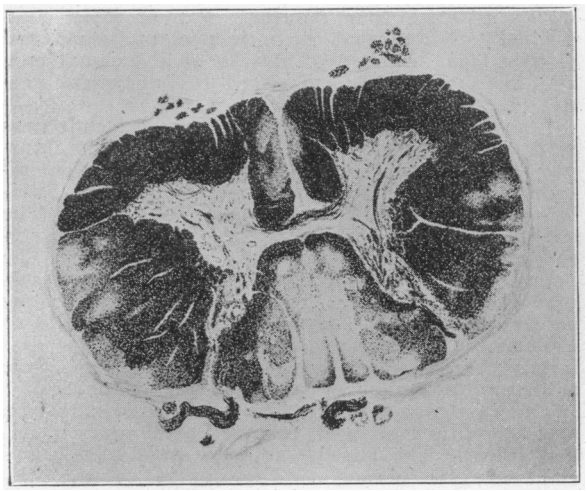
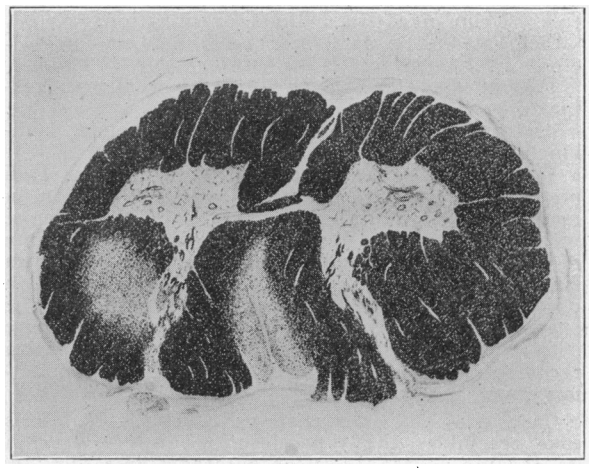
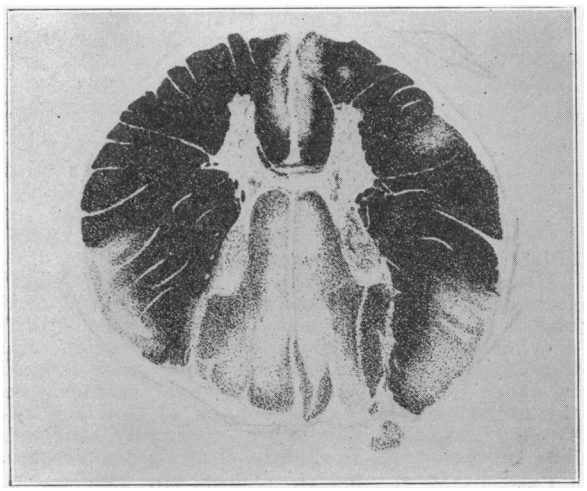
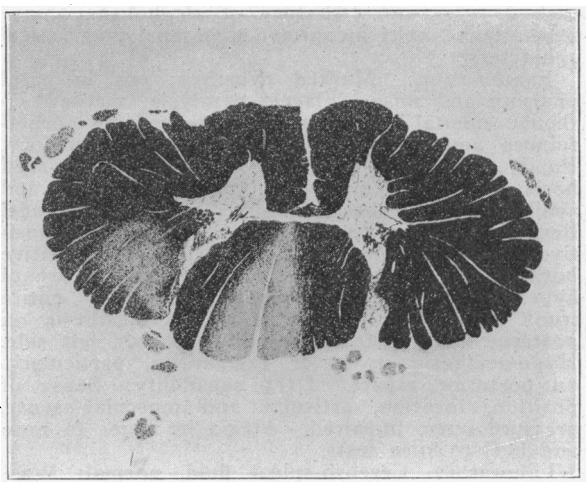
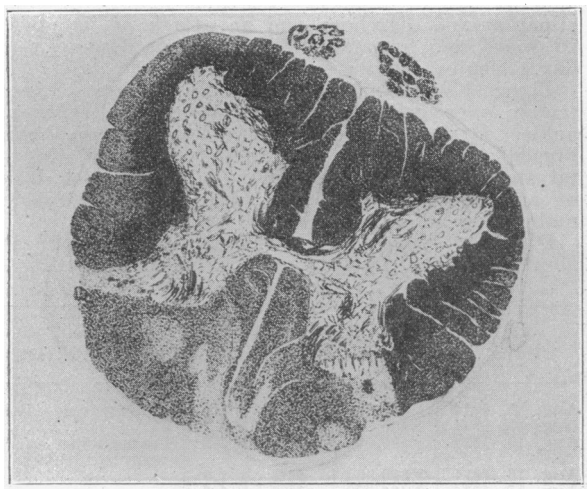
† The camera lucida drawings in this card series were made by my wife, Florence Crum Schaller, to whom I here wish to make acknowledgment.



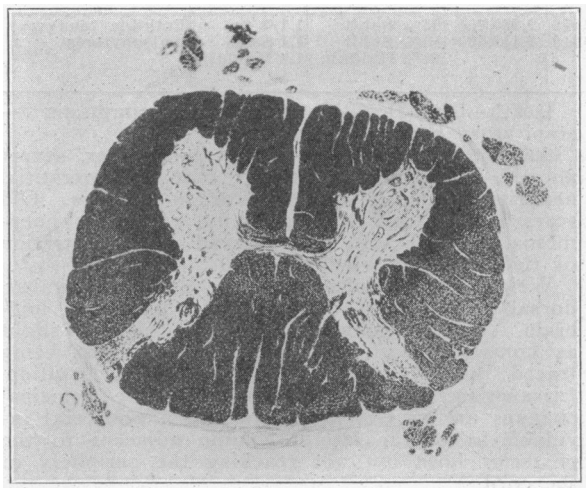








Case No. 1.—J. R. M., Dispensary No. 927, Combined Sclerosis. Weigert Stain of C-vi, D-ii, L-iii Cord.



Case No. 2.—J. K., Dispensary No. 11465-12, Combined Sclerosis. Weigert Stain of C, D, L Cord.

sermann in blood and cerebro-spinal fluid negative. Urine negative. Blood examination:

Date, March 14, 1913; Red cells, 3,520,000; Haemoglobin, 68%; Index, 0.9; Remarks, Poikilocytes few.

Patient died, March 21, 1912, of weakness, respiratory and cardiac failure.

Anatomical Diagnosis: Pernicious anemia, combined sclerosis, cystitis, acute pyelonephritis.

Weigert sections of cord (C-vi D-ii D-xi L-iii no sacral specimen) show marked degeneration in median parts of posterior white columns, most marked in, but not limited to, the median column of Goll. Marked quite irregular degeneration in lateral white columns and marked degeneration on either side of anterior longitudinal fissure. The sparing of the Lissauer zone is a striking feature of the histologic picture and in correlation with the sensory tests is in favor of this tract conducting touch sensibility.

Case 2. J. K. Dispensary No. 11465—12. This case resembles the type described by Gowers in its chronic course. Patient entered Clinic Oct. 16, 1912, age 51 years, complaining of weakness, difficulty in walking and numbness all over the body.

History of chancre at 21 years of age; 13 years ago paraplegia from which he never wholly recovered, but could walk without aid or support. Second attack of paraplegia 3 years ago, third attack 2 years ago. History of alcoholism. Since first attack slight incontinence of anal and vesical sphincters.

Examination: Marked pyorrhea; pus in nasal pharynx and nose. Flaccid paralysis; marked asthenia, mental deterioration evidenced by forgetfulness and lack of attention and emotionalism. Pupils react to light and accommodation; marked horizontal nystagmus both eyes. Patellar and achilles reflexes absent. Babinski, Gordon, Mendel Bechterew, Rossilimo negative. Oppenheim positive on right side (?), Strumpell's sign positive both sides. Sensibility disturbed in the nature of hyper-algesia, thermo-hyperaesthesia over entire trunk and upper extremities. Hyper-aesthesia on posterior part of trunk and upper thigh, left side. Hypo-aesthesia in lower extremities, particularly on posterior aspect. Deep sensibility: Sense of position, location, articular and muscular sense, pressure sense impaired. Ataxia in finger to nose and heel to knee tests.

Laboratory Cerebro-spinal fluid, normal; Wassermann negative, blood and cerebro-spinal fluid. Urine negative.

BLOOD REPORT.

Date	Red Cells	Haemoglobin	Color Index	Remarks
Oct. 18, 1912	2,250,000	60% Sahli	1.1/3	Poikilocytes few
Oct. 23, 1912	2,447,000	58% Sahli 64% Haldain	1.1 Sahli 1.3 Haldain	Anisocytosis

Death—Oct. 31, 1912, from bulbar symptoms ?—respiratory paralysis ?

Anatomical diagnosis: Cirrhosis of liver, severe anemia, combined sclerosis, chronic interstitial nephritis ?, arterio-sclerotic scars in kidneys. Old scars at both apices, emphysema hypostatic pneumonia, general adiposity, marked fatty infiltration of right heart, cholelithiasis.

Weigert and Kultschitzky sections of lumbar, dorsal and cervical cord, medulla, pons and midbrain. The degenerations are comparatively slight as compared with the preceding case, not being traced upwards from the pyramidal decussation. Lissauer's zone is not involved. The principal changes are in Goll's column and a unilateral involvement of the lateral column adjacent to the posterior horn but not reaching the periphery of the cord.

Case 3 (erroneously diagnosed clinically and at autopsy as tabes). G. D. Dispensary No. 10536—12. Patient entered Clinic Sept. 7, 1910, age 48 years, complaining of numbness in both feet and weakness since four months. Patient later complained of nocturnal incontinence of urine and pain in legs, and also of attacks of abdominal pain and diarrhoea, which appeared to be typical gastric crises.

Examination on entrance: Marked tenderness in region of gall-bladder, especially upon the Murphy manoeuver, marked distention in region inferior to the umbilicus. Gait ataxic; positive Romberg, absent patellar and achilles reflexes. The superficial sensibility was not impaired and the stereognostic sense in the hands was normal. The pupils reacted to light. Repeated blood Wassermanns were negative and two analyses of the cerebro-spinal fluid showed no increase in cells or globulin. The second fluid, however, showed a faintly positive Wassermann reaction. Patient gave a history of a chancre several years previously.

The case was diagnosed as tabes and was given anti-syphilitic treatment, followed by temporary improvement. The patellar reflexes were possible to elicit at this period. The course of the disease, however, was progressive. This patient died a suicide from a gunshot wound during an attack of mental aberration in the course of a lobar pneumonia.

Autopsy: Dec. 23, 1912, by Dr. Wm. Ophuls.

Anatomical Diagnosis: Tabes dorsalis—lobar pneumonia and bullet wound in forehead.

Blood Examination: Date, Aug. 22, 1912. White blood cells, 10,200.

White blood cells:

Polymorphonuclear	66%	per	c m m
Lymphocytes	26%	"	"
Large mononuclears	4%	"	"
Eosinophiles	2%	"	"
Basophiles			
Transitionals	2%	"	"

Date, Sept. 13, 1912. White blood cells, 8,200. (Blood examination incomplete.)

Histological examination of the cord: Weigert sections of sacral, lumbar, dorsal and cervical cord and at lower level of medulla showed symmetrical degenerations very slight in sacral region and limited to the lateral columns, and more intense in upper lumbar, dorsal and cervical regions. In the posterior columns the column of Goll and adjacent Burdach column are constantly affected. The Lissauer tract is slightly, if at all degenerated.

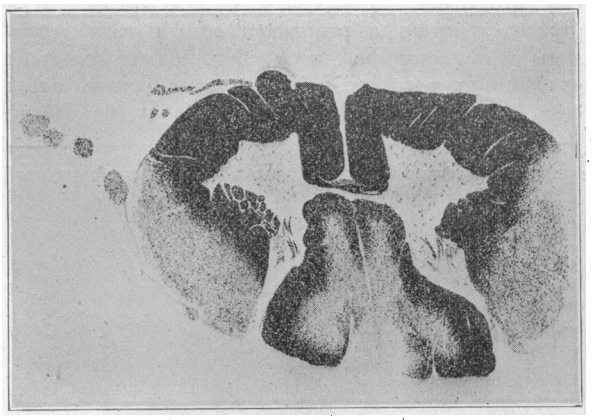
Case 4. M. S. Private records No. 236; age 49 years. Entered St. Luke's Hospital, San Francisco, Aug. 3, 1914. (History obtained from hospital records. Case not examined personally.) Duration of present illness 1½ years. Complaint: General weakness, periods of paresthesias, loss of appetite and drowsiness. Previous history of constipation and diarrhoea and an attack of jaundice; 16 years ago an attack of paraplegia lasting one day. Denies syphilis.

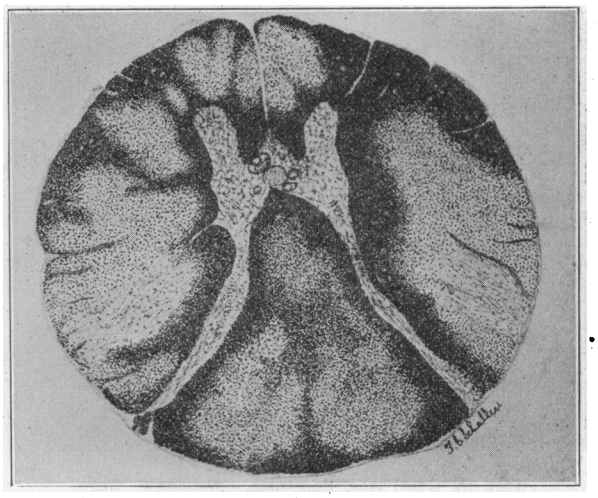
Physical examination: Anemic looking. Liver tender over gall-bladder. Lively tendon reflexes; ankle, patellar clonus, Babinski and Oppenheim present. Anesthesia below 10th, 11th dorsal. Mental state: Very complaining and irritable and lack of apprehension. X-ray findings denote probable malignancy of pyloric end of stomach.

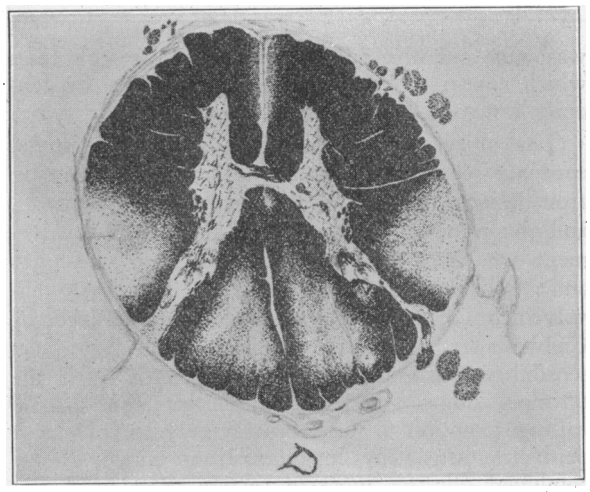
Probable diagnoses: Metastatic spinal tumor at about 9th, 10th, 11th dorsal. Transverse myelitis.

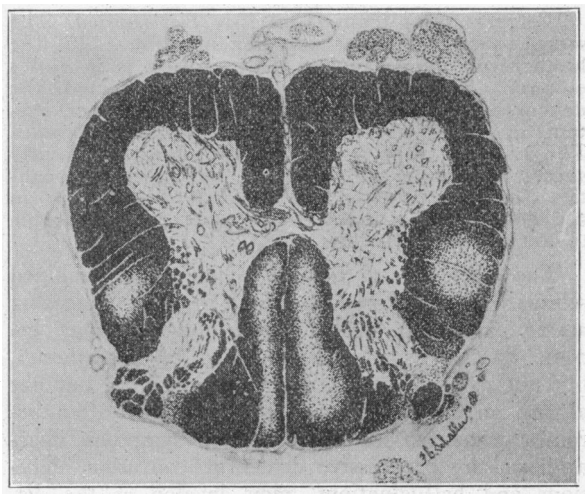
BLOOD REPORT.

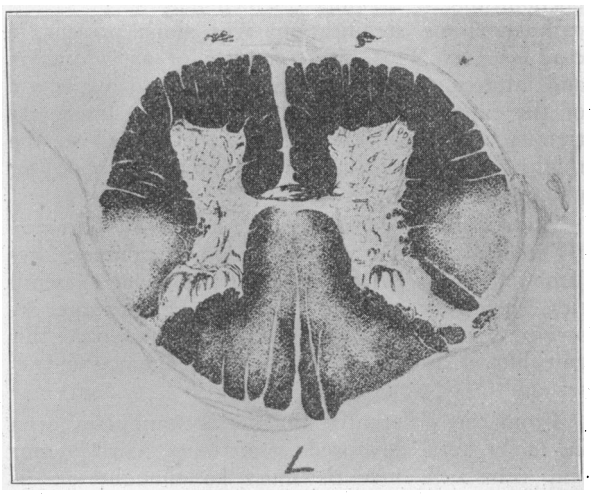
Date	Red Cells	Haemo-globin	Color Index	Remarks
Aug. 5, 1914.	1,500,000	35%	1.1	Anisocytosis—Poikilocytes
Aug. 13, 1914.	1,400,000	35%	1.2	
Aug. 15, 1914.	1,850,000	44%	1.2	Transfusion of blood, 16 min. duration
Aug. 16, 1914.	3,000,000	60%	1.0	
Aug. 17, 1914.	2,400,000	65%	1.3	
Aug. 21, 1914.	2,400,000	60%	1.2	
Aug. 28, 1914.	2,900,000	50%	1.3	



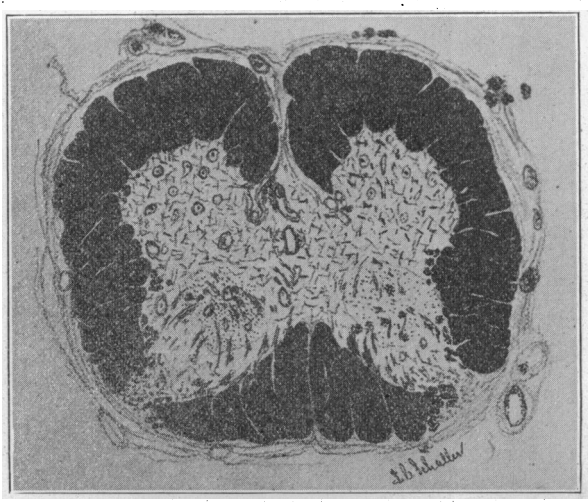




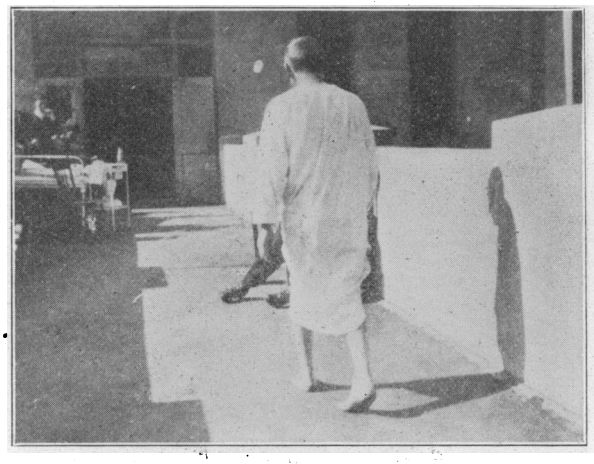




Case No. 3.—G. D., Dispensary No. 10536-12, Combined Sclerosis. Weigert Stain of C, D, L Cord.



Case No. 4.—M. S., Private Records No. 236, Combined Sclerosis. Weigert Stain of D-xii, L-iv, S-ii Cord.



Gait in Combined Sclerosis. Personal Case.

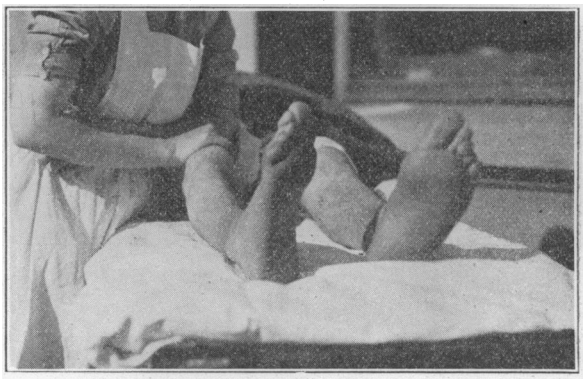
Patient died Sept. 3, 1914.

An incomplete autopsy was done, the lower portion of the cord only being removed.

Weigert stains from D-xii L-iv S-ii studied. The sacral sections show no degeneration. In the lumbar cord the principal degeneration is in Goll's column. The dorsal cord is greatly affected, the degenerations not being limited to any fiber system in the lateral and anterior white columns. The Lissauer zone in the lumbar region apparently shows a thinning of the fibers, but in other localities seems unaffected. The great destruction in the dorsal region assumes the severity comparable to a transverse myelitis.

The chief clinical features of subacute combined sclerosis will be seen to be a gradual increasing ataxic paraplegia, which later, however, may become flaccid, usually accompanied by paresthesias, but not pain. There is frequently at first, but not always an associated anemia which later often becomes pernicious in type. Mental symptoms characterized by progressive dementia, confusion, delusions and hallucinations, may develop as the disease progresses. The course of the disease varies greatly, running a protracted course with remissions as is exemplified in case No. 2, here reported; or running a rather rapid subacute course, as in case No. 1, in which the duration of the disease was nine months only. I have at present cases which appear to be arrested or improved. In general, however, I believe the prognosis to be grave.

Gait in Combined Sclerosis. (After Cruzon.)



Tibial Phenomenon of Strumpell.

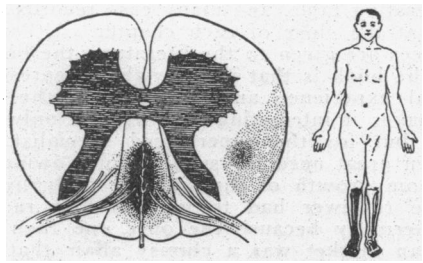
The objective symptoms referable to the spinal cord are seen to be a combination of those arising from lesions of both the lateral or pyramidal tracts, and the posterior columns. In this latter involvement we have disturbances of the deep sensibility and probable consequent ataxia. The early involvement of the bone sensibility emphasized by Cadwallader has been mentioned. The superficial sensibility is slightly, if at all, affected until the terminal stages. Dejerine emphasizes this fact in calling attention to the relatively early involvement of tactile sensibility in tabes from which disease combined sclerosis must in certain cases be differentiated (combined tabes). The motor symptoms are evidenced by weakness, increased muscle tonus, lively tendon reflexes and pathologic skin reflexes amongst which the Babinski, Oppenheim and Gordon may be mentioned. An important reflex, the tibial phenomenon of Strumpell which may be of almost pathognomonic signification, was alone present in case No. 2. This reflex consists of an adduction and internal rotation of the foot, due to overaction of the tibialis anticus muscle when the lower extremity is raised against resistance applied to the thigh, the patient lying in the supine position (see photograph).

A peculiar gait has been described by Crouzon (Thesis of Paris), called by him "trainment des jambes." This is a dragging of the lower extremities, somewhat similar to the hysterical gait described by Todd. One clinical case presented this gait but it is not of frequent occurrence in my series.

From the differential diagnostic standpoint even in fairly well advanced cases tabes, cord tumor and transverse myelitis must be thought of, as illustrated in the foregoing case histories. The condition most frequently confused, however, with subacute combined sclerosis is disseminated scle-

rosis. Bramwell dwells particularly on the points of difference between these two diseases. The diagnosis of combined sclerosis is particularly difficult in the early cases not associated with anemia. Such cases may easily be confused with a neurasthenic state on account of the paresthesias, lively inferior tendon reflexes, weakness, and the frequent association of gastro-intestinal symptoms. The following is an illustrative case in which combined sclerosis is strongly suspected.

A. W. Male, age 55 years, with complaint of several years' duration of "stomach trouble" and "heartburn." More recently patient has complained of nervousness and has also noticed a weakness and unsteadiness on feet and a peculiar tingling in the feet, hands and over entire body. His former physician had noted an increase in activity of the lower tendon reflexes which previously had been of normal intensity. The neurological examination, which included a cerebro-spinal fluid analysis and Wassermann tests, proved negative, with the exception of exceedingly lively tendon reflexes and a possible diminution in the bone sensibility in the lower extremities. The blood examination showed no anemia.



In combined sclerosis of the spinal cord associated with pernicious anemia the degeneration of the posterior columns is peculiar in that it begins in the more medianly situated fibers, that is to say, in the long fibers of the posterior columns, or Goll's columns, and in the parts adjacent to Burdach's columns. Consequently, in the early stages, deep sensation alone is disturbed, more particularly bone sensation and the sense of muscular position.

Diagram showing degeneration of the long fibers of posterior columns and disturbance of bone sensation. (After Cadwallader.)

CONCLUSIONS.

From the foregoing spinal cord examinations and from case records, the following points seem worthy of especial mention:

1. The cord changes in combined sclerosis are pseudo-system degenerations of toxic type. These degenerations in the posterior columns of the cord affect more particularly Goll's column and the adjacent portion of Burdach's, column sparing Lissauer's zone and the root entry zone. This localization explains the early involvement of the deep sensibility and conservation of the superficial sensibility.

2. With characteristic cord symptoms a pronounced anemia may not be present. In the absence of a low red blood count and low haemoglobin—an index above 1. is suggestive of a beginning pernicious anemia.

3. A focal infection is frequently found either in the buccal cavity or the gastro-intestinal tract.

Book Reviews

The Surgical Clinics of Chicago, Volume I Number V (October, 1917). Octavo of 214 pages 84 illustrations, Philadelphia and London: W. B. Saunders Company. 1917. Published bimonthly: Price per year, paper, $10; cloth, $14. Contents:

Dr. A. D. Bevan: Benign tumors of breast. Carcinoma of breast. Dr. A. J. Ochsner: Talipes equinovarus following acute anterior poliomyelitis. Varicose veins of leg. Postoperative tetany of sternocleidomastoid muscle. Dr. J. Ridlon: Hip disease. Dr. A. E. Halstead: Hereditary deformans chondral dysplasia. Dr. M. L. Harris: Hernia of breast. Dr. E. W. Andrews: Hemangioma of brain inoperable by ordinary methods. Dr. D. B. Phemister. Brain cyst following skull fracture. Dr. N. M. Percy: Partial evisceration through vagina during attempted abortion. Dr. C. Beck: Tendo- and neuroplasty. Elephantiasis and its treatment by Handley operation. Dr. H. L. Kretschmer: Hydronephrosis due to kidney stone. Ureteral calculus. Dr. T. J. Watkins: Cystocele, uterine prolapse, etc. Radium in hemorrhage at the menopause. Dr. D. N. Eisendrath: Complications of appendicitis. Clinical importance of congenital anomalies of kidney. Dr. H. McKenna: Perforated duodenal ulcer. Early recognition and treatment acute appendicitis. Dr. H. E. Mock: Case of bichlorid poisoning diagnosed and operated on as perforated gastric ulcer. Dr. D. C. Straus: Hammer toe. Dr. Kellogg Speed: Haematuria in appendicitis.

Radium Therapy in Cancer, at the Memorial Hospital, N. Y. (First Report, 1915-6). By Henry H. Janeway, with discussion of Treatment of Cancer of the Bladder and Prostate by B. S. Barringer, and an introduction upon the Physics of Radium by Gioacchino Failla. New York: Hoeber. 1917.

A résumé of the results of radium therapy during two years, in 424 cases of malignant tumors. Of these, 120 showed clinically complete retrogression, 134 were improved, 162 unimproved and fifty-nine were still under treatment. As a majority of the cases were classed as surgical derelicts and discards, the results may be considered as remarkable, and the author deplores the fact that more early cases do not receive the benefits of radium. The Memorial Hospital is fortunate in having about 2.8 gms. of radium, and the emanation is used in preference to the element. The technic of application and exposure time in each individual lesion is carefully given and particular emphasis is laid on the necessity of carefully screening for all except the most superficial lesions. In addition to the differential action of tumor cells whose susceptibility to radium are from two to seven times greater than that of normal tissue—the author believes that there may also be a stimulation of anti-cancerous activity of neighboring normal cells. Skin lesions, tumors of the parotid and the lymphosarcomas show the highest percentages of retrogression, while the carcinoma of the esophagus were the least encouraging. The difficulties in the treatment of the latter condition are fully described. Case history reports occupy a large part of the volume and it is regretted that more careful microscopical examinations could not be obtained in many of the cases, particularly those of the bladder and prostate. In these latter conditions radium probably offers the best therapeutic results. The introduction on the physics of radium and their close relation of the radiations to the Roentgen rays is carefully written and forms a valuable part of the book. This little volume should be of value to all interested in the treatment of malignant tumors, and particularly those attempting the use of radium. L. B.